I. 5-(α-PHENYLETHYL)-SEMIOXAMAZIDE AS A CARBONYL REAGENT

II. ANALOGS OF THE LUPIN ALKALOIDS

BY

JOSEPH HENRY BOYER

A.B., Hanover College, 1942

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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I. 5-(α-PHENYLETHYL)-SEMIOXAMAZIDE AS A CARBONYL REAGENT

A wide variety of carbonyl derivatives of semioxamazides containing substituents in the "5" position are without exception solid compounds which possess facile hydrolysis, thus permitting regeneration of the carbonyl compound.

Following Tierie's[1] procedure for the preparation of 5-phenylsemioxamazide, the reagent studied herein was obtained in an 83% yield by treating the condensation product between α-phenylethylamine and ethyl oxalate with hydrazine hydrate. The product, 5-(α-phenylethyl)-semioxamazide, easily formed derivatives with benzaldehyde, acetophenone, isobutyraldehyde, *n*-valeraldehyde, biacetyl, formaldehyde, cyclohexanone, cyclopentanone, 3-methylcyclohexanone, cycloheptanone, furfural, and cinnamaldehyde. Equimolar portions of the reagent and carbonyl compound were refluxed a few minutes in anhydrous benzene which contained a crystal of iodine. A number of complex carbonyl compounds failed to react under these conditions.

l-α-Phenylethylamine was obtained from the racemate by the method of Betti[2] and was used to prepare the optically active reagent. A successful resolution of 3-methylcyclohexanone by means of *l*-5-(α-phenylethyl)-semioxamazide gave *l*-3-methylcyclohexanone identified by the melting point and rotation of its semicarbazide.

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II. ANALOGS OF LUPIN ALKALOIDS

Leonard and Beyler[1] have recently synthesized sparteine

by hydrogenating the product of condensation between ethyl 2-pyridylacetate and ethyl orthoformate. It was desired to extend this synthesis to analogs of sparteine by substituting ethyl 2-quinolylacetate, ethyl 1-isoquinolylacetate, and ethyl orthoacetate.

Woodward and Kornfeld[2] have prepared ethyl 2-pyridylacetate by the condensation of phenyllithium and 2-picoline, followed by the addition of carbon dioxide, and esterfication. Application of this procedure to quinaldine failed. Instead it was found that phenyl-lithium added to the azomethine linkage of quinaldine.

Decarbonylation of ethyl 2-quinolylpyruvate by the method of Borsche[3] was found impractical on a large scale. Bachmann's[4] decarbonylation procedure using soft glass and iron filings had no effect. Dry pyrolysis gave an unidentified product.

Ring closure of N-(β-phenylethyl)-cyanoacetamide by means of polyphosphoric acid[5] was accomplished with hydrolysis and decarboxylation. The product was 1-methyl-3-4-dihydroisoquinoline instead of the desired 1-cyanomethyl-derivative which woul dhave led directly to ethyl 1-isoquinolylacetate.

Ethyl orthoacetate was prepared by the procedure of McElvain.[6] Condensation with ethyl 2-pyridylacetate failed to take place. From the reaction mixture was obtained, however, a new compound, the dimolecular cyclic dilactam of 2-pyridylacetic acid. It was later found taht this compound was formed in better yield from ethyl 2-pyridylacetate under basic conditions.

A recently reported alkaloid, *l*-pusilline,[7] probably resembles sparteins in structure. An attempt at its synthesis involved the Michael addition of ethyl 2-pyridylacetate to vinylpyridine. A reverse Michael, however, was postulated to account for the products, one of which was di-α-picolylmethane formd by th addition of picoline to vinylpyridine.

The octahydropyrrocoline nucleus occurs in a number of different alkaloid families including the lupin alkaloids.[8] It was found that aminopyruvic esters structurally similar to ethyl 2-quinolylpyruvate are reduced and cyclized over copper chromite to the corresponding substituted octahydropyrrocolines Quinaldine, 1-methylisoquinoline, 9-methylphenanthridine, 2-methylquinoxaline, 2,3-dimethylquinoxaline, and 1-benzyl-2-keto-1,2-dihydro-6-methylpyridine were allowed to condense with ethyl oxalate. The substituted pyruvic esters obtained thereby were reduced to the corresponding substituted octahydropyrrocolines.

Ethyl 2-quinolylpyruvate and the oximino-ester derived from it gave the same reduction product.

Ethyl *o*-nitrophenylpyruvate was reduced to N-ethyloctahydroindole instead of N-ethyldecahydroquinoline and the product was separated into its two racemic modifications.

Ethyl 4-quinolylpyruvate upon reduction formed 1,3-trimethylene-1,2,3,4-tetrahydroquinoline in a very small yield.

The condensation between 9-methylacridine and ethyl oxalate under the influence of potassium ethoxide failed to take place. Apparently an oxidation of the methyl group to an aldehyde group occurred. Condensation between the aldehyde and active methyl compound accounted for the product 1,2-di-(9-acridyl)-ethylene.

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VITA

The author was born at Otto, Indiana on January 4, 1922. He graduated from high school in 1938 and received the degree of Bachelor of Arts from Hanover College in 1942. Shortly after graduation he joined the USNR. Upon being released to inactive duty in June, 1946 he entered the Graduate School of the University of Illinois. From September 1946 to September 1949 he held a part-time assistantship in organic chemistry.

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